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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/633,699	08/05/2003	Pablo Umana	1975.0010004/TJS	5489

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EXAMINER	
BURKHART, MICHAEL D	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
01/05/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/633,699	UMANA ET AL.	
	Examiner	Art Unit	
	Michael Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *143-146,148-158 and 161-171* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *143-146,148-158 and 161-171* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/23/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/23/2010 has been entered.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 121 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See Transco Products, Inc. v. Performance Contracting, Inc., 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 09/294,584, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. See the 35 USC 112 1st ¶ rejection (New Matter) below. The instant claims are given a priority date of 8/5/2003, the filing date of the instant application.

Response to Arguments

Applicant's arguments filed 12/23/2010 have been fully considered but they are not persuasive. Applicants essentially assert that they are entitled to the priority date of the 09/294,584 application for reasons set forth in the response to the 35 USC 112-1st rejection below. Such arguments are considered to be answered below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 143-146, 148-158 and 161-171 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is maintained for reasons made of record in the Office Actions dated 10/31/2006, 11/15/2007, 2/3/2009, 11/25/2009, and for reasons set forth below. This is a New Matter rejection.**

Response to Arguments

Applicant's arguments filed 12/23/2009 have been fully considered but they are not persuasive. Applicants essentially assert that: 1) the instant specification shows that decreased fucosylation of antibodies results from expression of GnTIII; 2) the example of C2B8-25t provides support for the claimed subject matter as it has the highest levels of GnTIII expression and the highest

ADCC levels; 3) the Examiner is erroneous in inserting that applicants must rely upon inherent disclosure of the claimed subject matter;

Regarding 1) and 2), it is reiterated that because applicants do not have written, literal support for the claimed scope of antibodies, applicants must rely upon inherent disclosure of the claimed subject matter. It is further reiterated that the increase in ADCC for the CE7 and C2B8 antibodies was correlated with an increase in bisected complex oligosaccharides (column 27, lines 9-13), not a decrease in fucosylated oligosaccharides. This is probably because the sample with the greatest proportion of non-fucosylated oligosaccharides, CE7-15t, did not show an increase in ADCC (see Figs. 9 and 12 of the '084 patent). The antibodies presented in the instant application that had increased ADCC did not have a "majority" of nonfucosylated oligosaccharides, nor were they completely devoid of fucosylated oligosaccharides (within the scope of the instant claims). There is no analysis or discussion of what the actual "proportion of nonfucosylated oligosaccharides" inherently found on the antibodies of the specification might be. Analysis of the oligosaccharide profiles of the CE7-60t and -30t antibodies reveals that a majority of the oligosaccharides are fucosylated, in direct contrast to the instant claims. The antibody C2B8-25t, pointed to by applicants, was not analyzed for a glycosylation profile, hence, it is not certain that it comprises a an "increased proportion of nonfucosylated oligosaccharides." The closest example of a glycosylation progile of C2B8 would be that of the CE7 antibodies, already discussed at length and found not to provide support for the claimed subject matter. To review, the m/z 1689 and 1851 peaks of CE7 represent bisected complex oligosaccharides that are fucosylated, according to Fig. 11, the very peaks which led applicants to conclude that an increase in bisected complex oligosaccharides leads to an increase in ADCC (e.g. pages 36-39 of

the specification). Therefore, the passage cited by applicants, and Figure 9, supports the analysis above, that is, many of the antibodies comprised significant amounts (e.g. a majority) of fucosylated oligosaccharides, not non-fucosylated glycans. That fucosylation may be blocked by the action of GnTIII appears irrelevant in light of this data and the conclusions drawn by applicants in the specification linking increased ADCC with an increase in bisected complex oligosaccharides.

Regarding 3), tellingly, instead of pointing to actual, written support for the claimed subject matter, applicants must rely upon a complex analysis of the glycosylation profile of certain antibodies. There is no written conclusion by applicants that a broad link existed between nonfucosylated oligosaccahrides and ADCC, rather, as stated previously, applicants linked the increase in ADCC to increased bisected complex oligosaccharides.

Finally, applicants seek to claim a vast scope of antibodies using a single example of a single antibody that inherently has a decreased portion of non-fucosylated glycans. Just as many of the glycans analyzed have increased or no change in fucosylation for reasons of record. Applicants present no reasoning or evidence to refute this fact. Further, applicants present no discussion of the glycosylation profiles presented in the application, the strongest evidence of what the actual oligosaccharide structures on the CE7 antibodies are.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 143-145, 148-155, 157, 158, 161-167 and 169-171 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakamura et al (Cancer Res., 1994, cited by applicants) as evidenced by Shinkawa et al (JBC, 2003, of record) and Raju et al (Glycobiol, 2000, cited by applicants). **This rejection is maintained for reasons made of record in the Office Action dated 2/3/2009, 11/25/2009, and for reasons set forth below.**

Response to Arguments

Applicant's arguments filed 12/23/2010 have been fully considered but they are not persuasive. Applicants essentially assert that: 1) Nakamura et al do not teach a genetically glycoengineered antibody as instantly claimed, which is not to be considered a product-by-process limitation.

Regarding 1) applicants are asked how the structure of a glycoprotein can be directly modified genetically. They cannot be so modified directly according to the central tenets of molecular biology, i.e. genetic modifications directly effect nucleic acids, not proteins. That genetic modifications indirectly effect protein structure is stipulated, it is the point of the rejection. That is, the glycoproteins must be produced (i.e. a product-by -process) in cells or systems comprising the genetic modification. Further, the claims are so broad as to encompass the antibodies of Nakamura et al for reason of record. Therefore, the antibodies of Nakmura et al cannot be distinguished from those instantly claimed merely by how they were produced, as applicants assert. The YB2/0 cells of Nakamura et al have a different glycosylase expression profile than other types of cells (e.g. the teachings of Shinkawa et al) and produce antibodies

with glycosylation profiles within the scope of the instant claims. Thus, applicants assertions are unconvincing as the antibodies of Nakamura et al have a structure within the claimed scope.

Claim 143-146, 148-158, and 161-171 are rejected under 35 U.S.C. 102(b) as being anticipated by Umana et al. (WO 99/54342, cited by applicants). **This rejection is maintained for reasons made of record in the Office Action dated 2/3/2009, and for reasons set forth below.**

Response to Arguments

Applicant's arguments filed 12/23/2010 have been fully considered but they are not persuasive. Applicants essentially assert that Umana et al is not prior art because applicants are entitled to a priority date of 1998.

Such is not convincing for reasons set forth above. Applicants are entitled to a priority date of 8/5/2003 for reasons set forth above in the 35 USC 112 1st ¶ rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference

claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 143-146, 149-155, 157, 158, 161, 162, 164-167, and 169-171 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-22, 24-26, 34 and 35 of U.S. Patent No. 7,722,867. Although the conflicting claims are not identical, they are not patentably distinct from each other because the species of anti-EGFR antibody recited in the '526 claims anticipates, and thus renders obvious, the instant antibodies. EGFR is disclosed as inherently being expressed in several types of cancers (page 2 of the '526 specification).

This rejection is maintained for reasons made of record in the Office Actions dated 2/3/2009, 11/25/2009 (as US Application No. 11/348,526), and for reasons set forth below.

Response to Arguments

Applicant's arguments filed 12/23/2010 have been fully considered but they are not persuasive. Applicants request the rejection be held in abeyance. Hence, the rejection stands.

Conclusion

No claims are allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Burkhart whose telephone number is (571)272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Burkhart/
Primary Examiner, Art Unit 1633